REMARKS

Claims 2-4, 20-24 and 38-43 presently appear in this case. No claims have been allowed. The official action of December 4, 2002, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a protein comprising the amino acid sequence of SEQ ID NO:3, a variant of SEQ ID NO:3 which has at least 85% identity therewith, more preferably 90% identity and most preferably 95% identity, or a fragment of SEQ ID NO:3, or the variant thereof, all of which are capable of binding to TRAF2. The present invention further relates to compositions comprising such proteins and antibodies capable of binding thereto.

In the Office Action Summary, paragraph 4, the examiner states that claims 1-37 are pending in the application and that claims 5-19 and 25-37 are withdrawn from consideration. This is incorrect. At the time of the official action, only claims 1-4 and 20-24 were pending in the application and no claims were withdrawn from consideration.

It is noted that the examiner has agreed to examine all of the claims now present in the case.

It is noted that the examiner considers that claims 2-4 are not entitled to any of the claimed priority applications and, thus, have an effective filing date of September 28, 2000. It has also been noted that the examiner considers that claims 1 and 20-24 are entitled to the

effective filing date of September 1, 1998. In view of the fact that no intervening references have been cited, applicants reserve their traversal of this position of the examiner. Applicants' failure to traverse the holding of the examiner that claims 2-4 are only entitled to an effective filing date of September 28, 2000, is, thus, expressly made without dedication, disclaimer, waiver, forfeiture or estoppel. When and if the actual effective filing date becomes critical, applicants will express an opinion on the issue.

Claims 1 and 20-24 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which does not comply with the written description requirement thereof.

Claim 1 has now been deleted, and claims 20-24 have now been amended to become ultimately dependent from claim 2. As claim 2 is not subject to this rejection, it is believed that this rejection has now been obviated. Reconsideration and withdrawal thereof are, therefore, respectfully urged.

Claims 2-4 have been rejected under 35 U.S.C. §112, first paragraph as containing subject matter which does not comply with the written description requirement thereof. The examiner states that the claimed recitation of variants or fragments having an amino acid sequence that is at least 85% identical to SEQ ID NO:3 read on a broad genus of protein variants and that the specification does not disclose relevant

identifying functional characteristics of the variants/ fragment with respect the ability to bind to TRAF2 and the NF-κB regulatory complex. This rejection is respectfully traversed.

The examiner's attention is respectfully drawn to the Revised Interim Written Description Guidelines Training Materials and, particularly, Example 14: "Product-by-Function". In that example, the specification exemplified a protein isolated from liver that catalyzed the reaction of A→B, which isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO:3. The specification also contemplated, but did not exemplify, variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions, and additions. The specification indicated that procedures for making proteins with substitutions, deletions, insertions, and additions is routine in the art and provided an assay for detecting the catalytic activity of the protein.

This description in the specification is very similar to the description which appears in the present specification. The present specification exemplifies a NAP protein that binds TRAF2. The sequence of this protein is specified. The specification contemplates, but does not exemplify, variants of the protein wherein the variant can have substitutions, deletions, insertions, and additions. The present specification also indicates that procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art (see, for

example, page 50, line 12, to page 51, line 17) and provides an assay for determining whether any given protein binds to a specified binding protein. See, for example, the yeast two-hybrid method of Example 1 and the assay of Example 3. See also page 49, lines 19-23.

In Example 14 of the Training Materials, the claim is directed to:

> A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B.

The present claim 40 is drawn to a protein having SEQ ID NO:3 and variants thereof that are at lest 95% identical to SEQ ID NO:3 and have the ability to bind to TRAF2. Thus, this claim is substantially identical in format to that of the claim in Example 14 (fragments will be separately discussed below).

The analysis in the Training Materials acknowledges that procedures for making variants of SEQ ID NO:3 are conventional in the art and that an assay is described that will identify other proteins having the claimed functionality. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity were conceded as being conventional in the art.

The analysis goes on to point out that all variants of the claim must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO:3. Furthermore, because of the "comprises" language, the protein claimed may be larger than SEQ ID NO:3 or its variant with 95% identity to SEQ ID

NO:3. The analysis points out that the specification contains a reduction to practice of the single disclosed species. The analysis concludes:

> The specification indicates that the genus of proteins that must be variants of SEQ ID NO:3 does not have substantial variation since all the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
>
> Conclusion: The disclosure meets the requirements of 35 USC §112, first paragraph, as providing adequate written description for the claimed invention.

Thus, it is apparent that if the single species disclosed is representative of the genus and an assay is present for identifying the members of the variants which are capable of the specified functionality, the written description requirement is met, regardless of the protein chemistry arguments made by the examiner.

Furthermore, the examiner's comments about what effect a single amino acid change <u>might</u> have, does not really represent the state of the art. It is much more common that random changes will have no effect on the properties of the protein. Certainly, conservative changes would be expected to be tolerated.

Furthermore, many portions of a long protein have nothing whatsoever to do with the specific activity being claimed and, therefore, it would not be expected that changes in these portions would affect the functionality. It is unduly limiting to require an applicant to claim only the exemplified embodiments. Note *In re Goffe*, 191 USPQ 429, 431 (CCPA 1976), where it states:

> For all practical purposes, the board would limit appellant to claims involving the specific materials disclosed in the examples, so that a competitor seeking to avoid infringing the claims would merely have to follow the disclosure in the subsequently issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claim to what he has found will work or to materials which meet the guidelines specified to "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. See In re Fuetterer, 50 CCPA 1453, 1462, 319 F.2d 259, 265, 138 USPQ 217, 223 (1963)

It would not require undue experimentation to test any given analog to determine if it retains the properties of binding to TRAF2. Accordingly, as claim 40, and especially claim 43, are on all fours with Example 14 of the training materials, the present rejection must be withdrawn at least for these claims.

While Example 14 happens to select the number 95% for the purpose of its discussion, there is nothing therein that would suggest that this is some kind of a magic number. Indeed, one would expect that an identity of 90%, as is claimed in claims 39 and 42, or even 85%, as is claimed in claims 2 and 41, also

satisfy the written description requirement as all of the variants must possess the specified binding activity and must have at least 85% or at least 90% identity to the referenced sequence. Thus, the single species disclosed is representative of the genus because of the required structural similarity and because of the presence of an assay for identifying all of the at least 85% or at least 90% identical variants of SEQ ID NO:3 that are capable of the specified binding activity. Accordingly, for the same reasons that one would conclude that applicants were in possession of the necessary common attributes possessed by the members of the genus of variants having 95% identity to a specified sequence, so one of skill in the art could conclude that applicants were in possession of the necessary common attributes possessed by the members of the genus having 90% identity, or even 85% identity with SEQ ID NO:3. Accordingly, the present rejection should also be withdrawn for the remaining claims.

As to the "fragment" portion of the claim, it would be expected that if one amino acid were removed from the C-terminus that the fragment which remains will still be active. It is within the skill of the art to remove one amino acid at a time from either end of a protein or an analog, and then run the assay to determine if the fragment retains functionality. Once a fragment loses functionality, then it is not necessary to test any further. This does not involve undue experimentation. Thus, because any such fragment must have a portion of the specified sequence and a simple assay is readily available, as is a rational

means to determine which fragments would be expected to be operable, the full sequence, representing the single species of the NAP protein and its functional fragments, is representative of the genus. One of ordinary skill would thus conclude that applicants were in possession of the necessary common attributes possessed by the members of the genus. Therefore, the requirements of 35 U.S.C. §112, first paragraphs, as to providing adequate written description for the claimed invention are met. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 20 and 24 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The examiner states that the specification does not provide an enabled use for pharmaceutical compositions as claimed.

Claims 20 and 24 have now been amended to delete the term "pharmaceutical". It is urged that the remaining compositions have the same enabled use as the proteins. The claims no longer require a pharmaceutical utility. Accordingly, this rejection has now been obviated. Reconsideration and withdrawal thereof are, therefore respectfully urged.

Claims 1-4 and 20-24 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that the term "NF-κB regulatory complex" in claim 1 is a relative term that renders the claim indefinite

as it is not defined by the claim and the specification, such as at page 30, does not define all of the components of the NF-κB. The examiner states that without knowing what is and is not included in the "NF-κB regulatory complex" it is not impossible to know if a protein binds to it. This rejection is respectfully traversed.

Claim 2 has now been amended to delete reference to the NF-κB regulatory complex and require only that the protein bind to TRAF2. This is sufficient binding activity to identify relevant analogs of NAP. Furthermore, new claim 38 has now been added that defines the components of the NF-κB regulatory complex as defined at page 30 of the present specification. Accordingly, it is urged that none of the claims as presently amended would be subject to this rejection. Reconsideration and withdrawal thereof are respectfully urged.

Claim 1 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Claim 1 has now been deleted, thus obviating this rejection.

The references cited but not applied by the examiner have been noted, as has the examiner's implicit recognition that none of them are sufficient pertinent to warrant their application against the claims.

It is submitted that all the claims now present in the case clearly define over the references of record and

fully comply with 35 U.S.C. §112. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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